REMARKS

Rejection of the claims under 35 USC 112:

Claims 5-8 and 12-17 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants have amended to claims 5 and 12 to remove the indefiniteness. Applicants have described the formation of the claimed polymers on page 4 line 9 to page 5 line 12, in figures 1 and 2. Support for polymers capable of lysing mammalian cell membranes at pH 6.5 can be found on page 3 lines 13-21, page 5 line 29 to page 6 line 21, page 8 lines 18-29, and example 7 starting on page 14.

Rejection of the claims under 35 USC 102:

Claims 5-8 have been rejected under 35 U.S.C. 102(b) as being anticipated by Maeda et al. (US Patent 4,732,933).

Claims 5 and 12-14 have been rejected under 35 U.S.C. 102(e) as being anticipated by Tonge et al. (US Patent 6,436,905).

Claims 12-13 and 15-17 have been rejected under 35 U.S.C. 102(b) as being anticipated by Calcaterra et al. (US Patent 5,811,551).

Claims 12, 13, 15 and 16 have been rejected under 35 U.S.C. 102(b) as being anticipated by Smallman (BG 1241294).

Applicants have amended the claims to obviate the rejections. It is the Applicants' opinion that the prior art does not teach a membrane active styrene-maleic anhydride-based polymer or vinyl ether-maleic anhydride-based polymer capable of lysing mammalian cell membranes at pH 6.5. Applicants request reconsideration of the §102 rejections.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 5-8 and 12-15 should be allowable.

Respectfully submitted,

Kirk Ekena Reg. No. 56,672
Mirus Bio Corporation
505 South Rosa Road
Madison, WI 53719
608-238-4400

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as express mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this date: 5/26/05.

Kirk Ekena

in a 37 °C incubator. They were then spun for 1 min at 14,000 RPM. Lysis was determined by measuring the absorbance of the supernatant at 541 nm. Percent hemolysis was calculated assuming 100% lysis to be the absorbance of hemoglobin released upon addition of deionized water, all sample absorbances had the absorbance of buffer alone subtracted.

Example 8. Morpholino Delivery Assay: HeLa Tet-Off cells (Clontech Laboratories, Palo Alto, CA) were grown in Delbecco's Modified Eagle's Medium (DMEM, Cellgro, Herndon, VA) containing 10% fetal bovine serum (FBS) (Hyclone Laboratories, Logan, Utah) in a humidified incubator at 37°C with 5% CO_2 atmosphere. The cells were plated in 24-well culture dishes at a density of 3 x 10^6 cells/well and incubated for 24 hours. Medium was replaced with 0.5 ml DMEM, with or without 10% FBS, containing 0.5 µmol morpholino (CCT CTT ACC TCA GTT ACA ATT TAT A, SEQ ID [[10]] 1, Gene Tools, Philomath, OR) and either containing or not containing 20 µg of various polyanions. The cells were incubated for 4 hours in a humidified, 5% CO_2 incubator at 37°C. The media was then replaced with Dubelco's modified Eagle Media containing10% fetal bovine serum. The cells were then incubated for 48 h. The cells were then harvested and the lysate was then assayed for luciferase expression as previously reported [Wolff et al. 1990]. A Lumat LB 9507 (EG&G Berthold, Bad-Wildbad, Germany) luminometer was used. The amount of luciferase produced in the presence of morpholino and polyanion was normalized to the amount produced in the absence of polyanion and reported in Table 1.

Example 9. Synthesis of Disulfide-containing butyl amide of copolyvinylether-maleic anhydride (DBVEMA): To a solution of n-butylamine and cystamine (at a 50 to 1 molar ratio) in water is added 1 mol % eq (anhydride functional group of VEMA relative to amine groups) of VEMA. The solution is stirred overnight. The polymer is then precipitated out of solution by acidification with HCl to bring the pH to 2. The polymer is then isolated and dissolved again in water at pH 7.5 with $NaHCO_3$ in the presence of 10 molar equivalents of dithiothreitol (relative to starting cystamine). After 4 hours, the polymer is then precipitated out of solution by acidification with HCl to bring the pH to 2. The polymer is then isolated and dissolved again in water at pH 7.5 with $NaHCO_3$ in the presence of 10 molar equivalents of 2,2'-dithiodipyridine (relative to starting cystamine). After 4 hours, the polymer is then precipitated out of solution by acidification with HCl to bring the pH to 2. The polymer is then isolated and dissolved again in water. The presence of the thiopyridine is confirmed by measurement of the polymer's absorbance at 280 nm. The thiopyridine may used to conjugate